mide is frequently ingested with acetaminophen and codeine. This combination, called a "Doriden load," is favored by persons with narcotic addiction as a substitute for heroin. Glutethimide overdoses are often life-threatening. LSD is impregnated on postage-stamp-size colored pictures printed sequentially on transparent plastic ("transfers") or white porous paper ("blotters"). Drug abusers lick these "papers," transfer the picture to their skin and experience LSD intoxication. LSD is also poured over small pieces of pasta for street sale.

The preferred hallucinogen for "new wave rockers" is MDA (methylenedioxyamphetamine), which may be sold as very small—about 4 by 6 mm—flat, rectangular transparent chips of crystallized material called "window panes."

The use of amphetamines, including "look-a-likes" containing caffeine or phenylpropanolamine, is increasing, especially that of crystalline methamphetamine called "crank."

Intoxication from various sleeping pills and benzodiazepines continues. The leading cause of intoxication is still ethanol alone or in combination with another drug.

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Fine-Needle Aspiration Biopsy of the Prostate Gland

FINE-NEEDLE ASPIRATION has been used as a diagnostic tool since the beginning of this century. A mildly invasive technique, it has grown in popularity in the United States primarily on the basis of the ease and accuracy with which it can be used to obtain biopsy specimens to diagnose lesions in breast, superficial lymph nodes and thyroid. The prostate, however, is not so readily accessible and fine-needle aspiration of masses in this organ has not gained so ready an acceptance. After ten years' experience of doing this procedure on superficial lesions at the Karolinska Hospital in Stockholm, Dr Sixten Franzen in 1960 constructed a needle guide that makes the prostate easy to reach through the rectum using a 22-gauge needle.

The use of fine-needle aspiration is indicated when there is a suspicious, palpable lesion in a prostate. If a patient presents with distant metastasis for which the prostate may have been the source of the primary lesion, random aspirations of the four quadrants of the gland can be done. Not infrequently, such quadrant biopsy specimens will confirm the diagnosis of prostatic carcinoma. Lesions of clinically apparent prostatitis should not be aspirated.

With the Franzen needle guide, specimens can be taken of even very small (about 0.5 cm) and superficial lesions with a high degree of accuracy. Specimens from several different areas of the prostate can be taken without significant hemorrhage or other side effects. Fine-needle aspiration of the prostate is an outpatient procedure and does not require anesthesia. Patient discomfort is minimal, and patients readily accept a repeat biopsy if it is required.

In contrast, a core biopsy specimen obtained with a cutting needle requires local or general anesthesia and is less accurate, especially for small and superficial lesions in the posterior portion of the prostate. The sections from a core biopsy show only a fraction of the cells present in the specimen. An aspirate specimen almost always shows more cells for study than does that from core biopsy. In general, cellular detail on cytologic preparations from fine-needle aspiration is superior to the paraffin-embedded sections of a core biopsy.

The main disadvantage of this procedure is that there is a shortage of physicians in this country experienced in the biopsy technique and in the interpretation of the resultant smears. Good results cannot be obtained through reading about the technique and then attempting to do it; fine-needle aspiration must be learned under supervision, and the smears should be examined to ensure adequacy of the material.

After acquiring sufficient skill in the technique, it is still necessary to do at least five to ten aspirations a week. This is about the same degree of experience necessary to maintain skills in microscopic interpretation. Optimal results are obtained if the same physician does the aspiration and interprets the slides.

When performed and interpreted by a trained physician, fine-needle aspiration of the prostate gland is a highly accurate, fast and minimally invasive biopsy technique. There is a great need in this country for training programs to instruct physicians in the techniques of fine-needle aspiration of the prostate gland and other organs. If trained physicians are unavailable, it is better to rely on traditional histologic techniques. During the transition period between the use of traditional (core) biopsy and the implementation of fine-needle aspiration techniques, it may be feasible to do both procedures until such time as enough experience with the aspiration technique has been gained.

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Hepatitis—δ-Agent

THE RECENT DISCOVERY of a new hepatitis agent called delta (δ) marks the most exciting milestone since the identification of hepatitis A and B viruses nearly two decades ago. The δ-agent is a defective RNA virus, thus a virus taxonomically distinct from the hepatitis B virus (HBV) but requiring helper functions supplied by HBV. Hence, δ-hepatitis can occur *only* in the presence of HBV, and has three clinically recognizable forms: concomitant acute B and acute δ-hepatitis,

superinfection by the δ-agent in persons who are hepatitis B carriers and chronic δ-infection in a patient who has chronic hepatitis B.

Although simultaneous acute B and δ-infections can present as ordinary acute hepatitis, more often this dual infection results in a severe fulminant form.

δ-Superinfection in an HBV carrier may occasionally result in fulminant hepatitis but usually manifests itself as an acute icteric illness that is followed by chronic progressive liver disease. We now realize that the clinically evident, recurrent, hepatitis-like illness accompanied by jaundice that became more common during the late 1960s, which we all called chronic active hepatitis, was principally δ-modified chronic active hepatitis B. Data now show that, at least in the Los Angeles area, 82% of drug users with chronic active hepatitis B also have δ-infection.

Our clinical colleagues have noticed a difference in the manifestations of chronic active hepatitis in drug users as compared with ostensibly the same disease in homosexual men or in Asian immigrants. Similarly, we have been impressed with the general difference in "aggressiveness" of the hepatic histologic patterns in drug users versus nonusers who have chronic active viral hepatitis B. A major difference has been the presence of δ-superinfection, common in the former and uncommon (but increasing!) in the latter. It is likely that the histologic features of chronic active viral hepatitis that most pathologists have learned actually represent the dual infection. Serologic tests for δ-antibodies and immunologic staining for δ-antigen in the liver tissues establish the clinical diagnosis.

The δ-infection is described as endemic in Italy and sporadic in worldwide distribution. A major outbreak of cases of severe hepatitis due to δ-infection recently reported from South America should alert physicians to test for δ-markers in any new outbreaks of severe hepatitis.

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LD_6—A Biochemical Sign of Impending Death

AN EXTRA isoenzyme band of lactate dehydrogenase (LD) (EC 1.1.1.27) that is cathodic to LD_5 has been identified by several investigators. The underlying clinical condition is arteriosclerotic cardiovascular disease causing congestive heart failure with massive congestion of the major viscera. All of the patients had elevated total LD and creatine kinase (CK) levels. Serum enzyme electrophoresis showed that the LD_1 level exceeded or was equal to LD_2 and the CK-MB level was increased more than 5% as the acute myocardial infarcts evolved. As congestive heart failure became evident, a prominent amount of LD_5 became apparent, as did an LD_6 isoenzyme band cathodic to the LD_5 isoenzyme band. The ratio of blood urea nitrogen to creatinine was greater than 10:1 due to the progressive prerenal azotemia.

LD_6 is extremely stable at 56°C, 4°C and 25°C. It is not bound to an immunoglobulin and does not contain an H (myocardial) monomer but does contain an M (skeletal muscle) monomer. It may represent a posttranslationally modified LD_5.

LD_6 is not an artifact and most likely should be metabolized and cleared by a healthy liver and kidney. It is present and is identified when there is ischemia of the liver and kidney with circulatory failure. The appearance of LD_6 portends a very poor prognosis—as does the presence of creatine kinase mitochondrial isoenzyme—and is a sign of impending death.

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Heparin-Induced Thrombocytopenia and Thrombosis

DESPITE THE FACT that heparin is a powerful anticoagulant, it will infrequently induce thrombocytopenia and thromboembolic complications. Heparin-induced thrombocytopenia typically occurs about eight days after the institution of heparin therapy and is frequently followed by deep vein thrombosis, pulmonary embolism, arterial thromboembolic complications or a combination of these. Prior periods of heparin therapy will predispose some patients to the development of thrombocytopenia (less than 100,000 platelets per μl) as an anamnestic response within three to five days after reexposure. The episodes of arterial thrombosis or "white clot" syndrome frequently lead to infarction of end organs such as brain or heart or gangrene of an extremity. Although apparently ten times more likely to occur with bovine heparin than with porcine heparin, heparin-induced thrombocytopenia with thrombosis has occurred with both types. There does not appear to be a relationship to dosage, route or frequency of administration. The use of low-molecular-weight porcine heparin in this situation is promising but is still under study.

If the patient survives the thromboembolic complications, the platelet count usually returns to normal within two to four days after cessation of heparin therapy. Most patients who have been rechallenged with heparin after periods varying from a week to one year again manifested immediate thrombocytopenia.

In contrast to heparin-induced thrombocytopenia with thrombosis, there is a benign, mild depression of the platelet count that commonly occurs within two days after the institution of heparin therapy. Poorly understood, this type of heparin-induced thrombocytopenia is not mediated immunologically and requires no treatment. Although the reported incidence of both types of thrombocytopenia together reaches up to 30%,